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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/943,687	08/31/2001	Kamel F. Egbaria	MGP-104US	1264

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EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/943,687	EGBARIA ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGMENT TO AMENDMENT, REMARKS AND STATUS OF THE CLAIMS

1. The amendment and remarks filed 9/23/04 are acknowledged, entered and considered. In view of Applicant's request claims 1 and 14 have been amended. Claims 1-30 are now pending in the application. Applicant's contention that the Rule 132 declaration by Dr. Groves was procedurally and substantively sufficient to remove the Li et al reference from consideration is acknowledged. The contention presented in Applicant's response has been considered persuasive for the reasons set forth in the contention. Hence, the Examiner confirms the removal of Li et al reference from consideration. However, the rejection under 35 U.S.C. 103(a) over the prior art of record is maintained for the reasons of record.

ARGUMENTS ARE NOT PERSUASIVE

CLAIM REJECTIONS-35 U.S.C. § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-30 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Cho et al (U.S. Patent No. 5,962,019) taken with Charman et al (Pharmaceutical Research, Vol. 9, No. 1, pp. 87-93, 1992) and Kovacs et al (U.S. Patent No. 5,583,105).

Applicant's arguments filed 9/23/04 have been fully considered but they are not persuasive. Applicant has argued that Charman et al is silent regarding a corticosteroid forming a spontaneous emulsion, let alone cyclosporin as claimed in amended claim 1. Although, WIN 54954 is lipophilic and cyclosporin may be lipophilic, Applicant submits that such a disclosure in Charman et al does not teach each and every limitation of the claimed invention. Applicant concludes by stating that Charman et al fails to fill the void of Cho et al and Kovacs et al, the combination of the cited references cannot be said to render obvious the claimed invention is unpersuasive. Contrary to Applicant's arguments, the Examiner has clearly indicated as discussed in the previous Office action that the primary reference of Cho et al teaches an orally administered pharmaceutical composition comprising cyclosporin (including cyclosporin A), ethanol,

polyoxyethylene compounds and polyoxyethylene derivatives of fatty acids (which includes polyoxyethylene glycerol trioleate), and an oil component (such as ethyl oleate) and a method of preparing such pharmaceutical formulation thereof. The reference discloses various concentrations for oral cyclosporin formulation, wherein the preferred concentration for cyclosporin A ranges from 50 to 150 mg/ml, for alkanols such as ethanol ranges from 5 to 60% (v/v), for oil component such as ethyl oleate ranges from 15 to 75% (v/v), and for polyoxyethylene compounds or derivatives thereof ranges from 5 to 60% (v/v). (See cols. 3-7 and the claims) as directed to claims 1-13 and 18-26.

Applicant alleges that Cho et al does not teach a spontaneous formulation, let alone a spontaneous emulsion having the specified diameter of particles, or the specified concentrations, or the specified ratio of the components as claimed in the present invention is unpersuasive. Contrary to Applicant's allegation the '09 patent of Cho et al on col. 7, lines 15-29 suggests by stating that the subject formulations may also be prepared as aqueous colloidal dispersions of cyclosporin nanoparticles, having good bioavailability. It is conventional and known in the art that colloidal dispersion is by definition is emulsion (See e.g., for support page 460, Table 12.6 of General Chemistry, Fifth Edition, published by HBJ, 1988). Thus, the '019 patent clearly suggests the formulations of spontaneous emulsion with the diameter of the particles of said spontaneous emulsion and the specific concentrations and ratios recited in the claims because the ranges disclosed by the reference overlaps with the claimed ranges. Further, on Applicant's response filed 9/23/04 on page 7, last paragraph Applicant has admittedly acknowledges that WIN 54954 is lipophilic and cyclosporin may be lipophilic.

Thus, in view of the acknowledgements, the secondary reference of Charman et al discloses a formulation of a lipophilic compound WIN 54954, in a medium chain triglyceride oil/nonionic surfactant mixture, which exhibited self-emulsification under conditions of gentle agitation in an aqueous medium. The resulting oil/water emulsion produced spontaneously because self-emulsifying drug delivery systems (SEDDS) are thermodynamically stable, as opposed to the regular emulsion, which are thermodynamically unstable. The resulting formulation produced dispersion with mean droplet diameters of less than 3 μm, which is about 3000 nm because 1 μm = 1000 nm. Thus, having a diameter of less than 3 μm (i.e., 3000 nm) would include the recited diameter ranges 50 to 185 nm of claims 17 and 28, and 50 to 150 nm of claims 29 and 30 (See e.g., pages 87-88 and 92) as directed to claims 16, 17 and 28-30. Thus, clearly showing that self-emulsifying drug deliver systems (SEDDS) are a convenient method of delivering hydrophobic drugs with a formulation of a spontaneous emulsion having specific diameter.

With respect to the selection of specific concentrations and ratios as recited in the claims, although, all the references show the ranges claimed, however, Kovacs et al discloses the specific and preferred concentration ranges and ratios as claimed in the instant invention (See e.g., cols. 1-4 and claims 1 and 8-12) as directed to claims 1-15 and 18-27. Although, none of the prior art cited alone teaches each and every limitations of the claimed invention, however, the combined teachings of the prior art would have motivated one of ordinary skill in the art at the time the invention was made to apply the teachings of the secondary references (i.e., the formulation of spontaneous

emulsion with the diameter of the particles of said spontaneous emulsion and the specific concentrations and ratios recited in the claims) to the primary reference teachings of orally administering pharmaceutical composition comprising cyclosporin (including cyclosporin A), ethanol, polyoxyethylene compounds and polyoxyethylene derivatives of fatty acids (which includes polyoxyethylene glycerol trioleate), and an oil component (such as ethyl oleate) and a method of preparing such pharmaceutical formulation thereof because such features are known or suggested in the art, as seen in the secondary references, and including such features into the primary reference would have been obvious to one of ordinary skill in the art to obtain the known and recognized functions and advantages thereof

Therefore, the combined teachings of the prior art makes obvious the claimed invention's orally administered pharmaceutical composition in a form of a spontaneous emulsion comprising cyclosporin (cyclosporin A), ethanol, polyoxyethylene glycerol trioleate, and an oil component (ethyl oleate) and a method of preparing such pharmaceutical formulation thereof. Thus, it is made obvious by the combined teachings of the prior art since the instantly claimed invention which falls within the scope of the combined teachings of the prior art composition and method would have been *prima facie* obvious from said prior art disclosure to a person of ordinary skill in the art because as held in host of cases including *Ex parte Harris*, 748 O.G. 586; *In re Rosselete*, 146 USPQ 183; *In re Burgess*, 149 USPQ 355 and as exemplified by *In re Best*, "the test of obviousness is not express suggestion of the claimed invention in any

and all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them".

OBJECTION TO THE TITLE, SPECIFICATION, ABSTRACT AND CLAIMS

3. The title, specification, abstracts and the claims are objected in the recitation "cyclosprine". It is believed the correct spelling is "cyclosporin". See e.g., the '019 patent of Cho et al. Appropriate correction is required.

ACTION IS FINAL

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

CONCLUSION AND FUTURE CORRESPONDANCE

5. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272 0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (571) 272 0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JON WEBER
SUPERVISORY PATENT EXAMINER

Mohamed/AAM
December 8, 2004